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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/498,046 | 02/04/2000 | Sabine Neirynck | VIB-08 | 8244 |

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Husch Blackwell Sanders, LLP
Husch Blackwell Sanders LLP Welsh & Katz
120 S RIVERSIDE PLAZA
22ND FLOOR
CHICAGO, IL 60606

| EXAMINER | |
|---|---|
| CHEN, STACY BROWN | |
| ART UNIT | PAPER NUMBER |
| 1648 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/498,046 | NEIRYNCK ET AL. | |
| | Examiner | Art Unit | |
| | Stacy B. Chen | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *18 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *26,31,32,34,36-41,46,52-56,58,60 and 61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,31,32,34,36-41,46,52-56,58,60 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/27/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 18, 2009 has been entered. Claims 26, 31, 32, 34, 36-41, 46, 52-56, 58, 60 and 61 remain pending and under examination.

### *Response to Amendment*

2. The rejection of claims 26, 31, 32, 36, 38, 41, 46, 53, 54 and 57-61 under 35 U.S.C. 103(a) as being unpatentable over Pumpens (*Intervirology*, 1995, 38:63-74, "Pumpens") in view of Slepushkin *et al.* (*Vaccine*, 1995, 13(15):1399-1402, "Slepushkin") as applied to claims 26, 31, 32, 36, 38, 41, 46 and 53-55 above, and further in view of Sunstrom *et al.* (*J. Membrane Biol.* 1996, 150:127-132, "Sunstrom", already of record) or Hongo *et al.* (*Journal of Virology*, April 1997, 71(4):2786-2792, "Hongo"), is withdrawn in view of Applicant's amendment. The claims no longer recite embodiments relating to NB and CM2 proteins.

### *Claims Summary*

3. The claims are drawn to a human influenza immunogenic composition comprising a fusion product. The fusion protein has an antigen consisting essentially of an immunogenic extracellular part of an M2 membrane protein of a human influenza A virus, and a heterologous

peptide or polypeptide presenting carrier. The carrier is selected from the group consisting of hepatitis B core protein, C3d, polypeptides comprising multiple copies of C3d and tetanus toxin fragment C.

Chapter 2111.03 of the MPEP [R-3] provides guidance on the use of transitional phrases "comprising", "consisting essentially of" and "consisting of" as they define the scope of a claim with respect to what unrecited additional components or steps, if any, are excluded from the scope of the claim. The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. In the instant claims, the antigen portion of the fusion protein that consists essentially of an immunogenic extracellular part of an M2 membrane protein of a human influenza A virus, is understood by the Office to be an antigen *comprising* an immunogenic extracellular part of an M2 membrane protein of a human influenza A virus. The reason that the Office interprets the antigen to *comprise* the immunogenic extracellular part of M2, is that the specification fails to define the metes and bounds of the antigen that *consists essentially of* an immunogenic extracellular part of an M2 membrane protein.

### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 26, 31, 32, 36, 38, 41, 46, 53-56 and 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pumpens (*Intervirology*, 1995, 38:63-74, "Pumpens") in view of Slepushkin *et al*. (*Vaccine*, 1995, 13(15):1399-1402, "Slepushkin"). Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that the motivation to combine the teachings of Pumpens with Slepushkin is inadequate. Particularly, Applicant argues that the statement by Slepushkin concerning the vaccinia-M2 recombinants being unable to provide protection in mice is not motivation to combine Slepushkin's M2 with Pumpens HBc carrier. Applicant reasons that Slepushkin did demonstrate protection from influenza with the M2 composition, thus overcoming the problems of the prior art; therefore, there would have been no apparent motivation to further modify the M2 composition of Slepushkin.
  - In response to Applicant's arguments, the obviousness rejection follows this logic: Pumpens discloses HBc carriers that are useful as epitope carriers. Pumpens does not specifically name the influenza A M2 antigen. However, Slepushkin discloses influenza A M2 antigen and also teaches that there are problems with protective immunity when using the M2 antigen in certain contexts, such as the vaccinia-M2 recombinants. Therefore, given the problems associated with inducing an effective immune response using M2, it would have been obvious to use a system of presenting M2 to the immune system that would enhance its immunogenicity. Slepushkin found that partially purified baculovirus-expressed M2 worked, but that is not the only way to increase the immunogenicity of M2 available in the art. The test for obviousness is

not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference. Considering Pumpens' teachings regarding the advantages of using HBc carriers, one would have been motivated to increase the immunogenicity of M2 by using the HBc carrier.

- Applicant argues that Slepushkin suggests the use of the full-length M2 protein, whereas the instant invention employs an extracellular part of M2 (M2e). Applicant disagrees with the Office's reasoning for the obviousness of using the extracellular portion of the M2 protein. Applicant asserts that viral antigenic peptides from all viral proteins are presented to the immune system, pointing to Slepushkin (Table 2) which shows that the strongest antigen response was generated to an intracellular epitope of M2, PM8, not the extracellular portion of the M2 protein.
  - In response to Applicant's argument, the claims are not limited to an extracellular part of M2, as explained above in the "Claims Summary" section. In the instant claims, the antigen portion of the fusion protein that consists essentially of an immunogenic extracellular part of an M2 membrane protein of a human influenza A virus, is understood by the Office to be an antigen *comprising* an immunogenic extracellular part of an M2 membrane protein of a human influenza A virus. The reason that the Office interprets the antigen to *comprise* the immunogenic extracellular part of M2, is that the specification fails to define the metes and bounds of the antigen that *consists essentially of* an immunogenic extracellular part of an M2 membrane protein. The specification does not indicate exactly what is excluded from or what interferes with the immunogenicity of an extracellular part of an M2 protein.

- Even if Applicant's specification adequately defined what is excluded from an antigen "consisting essentially of" an immunogenic extracellular domain of an M2 protein, the prior art's protein still reads on the claimed invention because the full-length M2 protein contains the immunogenic extracellular domain, and there is no indication that the remaining portions of the full-length protein interfere with the extracellular domain's immunogenicity.
- Furthermore, even **if** the claims were limited to the extracellular part of M2, it would have been obvious to use the extracellular part of this protein because it is more exposed initially to the immune system than the intracellular part of the protein. While the immune system processes and presents peptides from various parts of the virus, the immune system must first recognize the virus as being non-self, and then respond appropriately. The proteins that are exposed on the virion include the extracellular portion of the M2 protein. The Office is not saying that the immune response to the extracellular portion of M2 would be the only valuable response, or that such a response would be protective, rather, that the response to the extracellular portion of the M2 protein would be valuable because it is readily exposed to the immune system upon infection.

6. Claim 37 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Pumpens (*Intervirology*, 1995, 38:63-74, "Pumpens") in view of Slepushkin *et al.* (*Vaccine*, 1995, 13(15):1399-1402, "Slepushkin"), as applied to claim 26, and further in view of Highfield *et al.*

(AU-B-49273/90, "Highfield", cited in IDS filed 11/26/07). Applicant's arguments have been addressed above.

7. Claims 34 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pumpens (*Intervirology*, 1995, 38:63-74, "Pumpens") in view of Slepushkin *et al*. (*Vaccine*, 1995, 13(15):1399-1402, "Slepushkin"), as applied to claim 26, and further in view of Highfield *et al*. (AU-B-49273/90, "Highfield") and van de Guchte *et al*. (*Applied and Environmental Microbiology*, 1989, 55(1):224-228, "van de Guchte"). Claims 34 and 39 require that the immunogenic composition comprise *Lactococci* cells expressing the fusion product in or on their cell membrane or cell well. Applicant's arguments have been addressed above.

8. Claims 40 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pumpens (*Intervirology*, 1995, 38:63-74, "Pumpens") in view of Slepushkin *et al*. (*Vaccine*, 1995, 13(15):1399-1402, "Slepushkin"), as applied to claim 26, and further in view of Kedar *et al*. (U.S. Patent 5,919,480, filed June 23, 1997, "Kedar"). Applicant's arguments have been addressed above.

***Conclusion***

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/
Primary Examiner, TC1600